Remarks

Claims 1-18 are pending in this application. Claims 14-18 have been canceled without prejudice. No new matter has been added as a result of the above amendments.

Drawings

An appropriate amendment has been made to include the sequence identity for figure 1.

Claim Objections

Claim 1 is objected to because the claim contains more than one period. An appropriate amendments has been made to claim 1.

Rejection of claims 5 and 9 under 35 USC § 112, second paragraph

Claims 5 and 9 are rejected under 35 USC § 112, second paragraph. Applicant respectfully disagrees. Specifically, claim 5 is alleged to be indefinite with respect to the recitation of "no-selective with respect to the template." The Examiner states that it is unclear whether claim 5 further limits claim 4 or whether the claim in intended to modify QB replicase to be non-selective in some way.

Applicant has amended claim 5 to further clarify what is being claimed. The intention of Applicant is to make clear that the RNA polymerase that is claimed is not selective with respect to any particular replicatable RNA template recited in claim 1. If Applicant still has not satisfied the Examiner's concern, Applicant requests further clarification by Examiner and she is invited to call the undersigned attorney.

Claim 9 is alleged to lack proper antecedent basis because the term "the composition of the vessel" is unclear. Applicant has amended claim 9 to alleviate Examiner's concern.

Applicant respectfully requests reconsideration and withdrawal of the present rejections.

Rejection of claims 1-13 are rejected under 35 USC 102(b)

Claims 1-13 are rejected under 35 USC 102(b) as being anticipated by Brown *et al.* (Biochemistry, v34, 1995, pp. 14775-782) as evidenced by Brown-2 *et al.* (Biochemistry, v34, 1995, pp. 14765-774). Applicant respectfully disagrees.

The Examiner asserts that Brown teaches a method of selection and characterization of RNAs replicated by QB replicase. The Examiner continues, "Brown teaches a method of making a replicable RNA template having a selected affinity to a target comprising applying a selection to a first generation comprising a replicatable RNA template using a RNA polymerase to form replicatable RNA templates where the selection is based on the affinity of replicatable RNA template of different generations to said target."

Section 102 of Title 35 provides the novelty requirements for patentability. In order for a prior art reference to anticipate a claim it must teach each and every element of that claim. M.P.E.P. §2131. The Court of Appeals for the Federal Circuit states:"[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628 (CAFC, 1987).

The presently claimed invention discloses a method of making replicatable RNA templates which have a high affinity to a heterogenous or target through iterative steps. For conceptual purposes, one can consider the target analogous to a trans-acting element. This trans element target however becomes attached to the polymerase. Unlike Brown, the claimed invention employs heterogenous target molecules in order to screen the RNA templates. For example, the Examiner is directed to page 4 the first full paragraph. Line 10 is a good example of the heterogeneous nature of the target of the present invention. Beginning on line 10 it reads, *sic* "[t]he target is bound to or incorporated in onone or more subunits [referring to the subunits of the polymerase." Continuing on line 11, ... the target is a protein the nucleic acid encoding such target is cloned into the nucleic acid

encoding such subunit [again referring to a subunit of the polymerase] and expressed as part of such subunit." So unlike Brown, the target in the claimed invention refers to a molecule that is not originally part of the polymerase - to put it in molecular terms, the nucleotide sequence encoding the unmodified polymerase lacks sequence coding for a target. In Brown there is no corresponding heterogenous target molecule bound to or encoding within the polymerase.

The selection for the claimed invention is based upon the affinity between an RNA replicatable template and the heterogenous target. In Brown, the selection process actually involves selecting RNAs of appropriate lengths, see, for example, pg 14776, column 1, lines 9ff, same page column 2, lines 25ff, and pp 14777-8, starting at column 2, line 3 and over to the next page. The efficiency of RNA replication was also dependent upon how well the RNA bound to the enzyme itself, not any heterogenous target attached thereto. The binding affinity that Brown speaks of is essentially the binding affinity one speaks of in terms of enzyme kinetics and not as the claimed invention employs the term viz. a target molecule.

Brown-2 suffers from the same deficiency as Brown-1. By utilizing the SELEX selection process, the deficiency is not overcome. This selection process exploits the binding affinity between an RNA molecule and polymerase. Again, there is no heterogenous target molecule, as in the claimed invention, that is used in the selecting for high affinity RNA molecules.

Therefore, Brown-1 alone or even in combination with Brown-2 fails to teach each and every element of the presently claimed invention. Hence, Applicant respectfully requests reconsideration and withdrawal of the present rejection.

Rejection of claims 1-13 are rejected under 35 USC 102(b)

Claims 1-13 are rejected under 35 USC 102(b) as being anticipated by Kawasaki (US Pat. No. 5,643,768) as evidenced by Brown-2 *et al.* (Biochemistry, v34, 1995, pp. 14765-774). Applicant respectfully disagrees.

The Examiner asserts that Kawasaki teaches a "method of making a replicatable RNA template having a selected affinity to a target comprising applying a selection to a first generation comprising a replicatable RNA template using a RNA polymerase to form replicatable RNA templates where the selection is based on the affinity of replicatable RNA template of different generations to said target."

Actually, Kawasaki discloses a method for a cell-free synthesis and isolation of novel genes and polypeptides where a nascent polypeptide binds to "a substance of interest." This substance of interest could be an antibody specific for the nascent polypeptide. In Kawasaki's method an expression unit comprising a nucleotide sequence capable of interacting with a ribosomal unit is "attached" to a random nucleotide sequence. This newly formed nucleotide complex is then transcribed forming an RNA molecule. This RNA (mRNA) molecule is then translated and hence complexes with one or more ribosomal units forming a polysome. The polysome synthesizes nascent polypeptides. These nascent polypeptides are then introduced to "substances of interest." The substance of interest is available for binding to the polypeptide should appropriate affinity exist between the substance of interest and the nascent polypeptide. For example, the substance of interest could be an antibody. Assuming that there exists sufficient affinity between the substance of interest and the nascent polypeptide, then a complex is formed between the two. The polysomes that are not complexed can be discarded, thus allowing for only the complexed polysomes to remain. The RNA can be retrieved and from that cDNAs are formed and amplified, thus increasing the number of nucleotide sequence of interest.

Applicant's claimed invention is significantly different from that disclosed in Kawasaki. For instance, in the presently claimed invention, selection is based upon the affinity between an RNA replicatable template and the heterogenous target, not a translated product and the heterogenous target. Moreover, the presently claimed invention is not concerned with a translated product, whereas in Kawasaki, it is the translated product, the polypeptide, that plays a vital role in the selection process.

With regard to Brown-2, please refer to the discussion above. Suffice it to say, Brown-2 does not remedy the deficiencies present in Kawasaki. Therefore, Kawasaki alone or in combination with Brown-2 fails to teach or suggest each and every element of the instantly claimed invention.

Applicant respectfully requests reconsideration and withdrawal of the present rejection.

Applicant believes that his claimed invention is now in condition for allowance and respectfully requests that the Examiner issue a Notice of Allowance. The Examiner is invited to call the undersigned attorney at (617) 854-4237 should she determine that a telephonic interview would expedite prosecution of this case.

Respectfully submitted,

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